

SEQUENCE LISTING

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Nelboeck-Hochste, P.
Schoenfeld, H.

<120> MODIFIED PHOSPHODIESTERASE POLYPEPTIDES WITH ALTERED PHYSIOCHEMICAL
PROPERTIES

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<151> 2002-12-17

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Met Thr Ser Pro Gly Ser Gly Leu Ile Leu Gln Ala Asn Phe Val His

35 40 45

Ser Gln Arg Arg Glu Ser Phe Leu Tyr Arg Ser Asp Ser Asp Tyr Asp
50 55 60

Leu Ser Pro Lys Ser Met Ser Arg Asn Ser Ser Ile Ala Ser Asp Ile
65 70 75 80

His Gly Asp Asp Leu Ile Val Thr Pro Phe Ala Gln Val Leu Ala Ser
85 90 95

Leu Arg Thr Val Arg Asn Asn Phe Ala Ala Leu Thr Asn Leu Gln Asp
100 105 110

Arg Ala Pro Ser Lys Arg Ser Pro Met Cys Asn Gln Pro Ser Ile Asn
115 120 125

Lys Ala Thr Ile Thr Glu Glu Ala Tyr Gln Lys Leu Ala Ser Glu Thr
130 135 140

Leu Glu Glu Leu Asp Trp Cys Leu Asp Gln Leu Glu Thr Leu Gln Thr
145 150 155 160

Arg His Ser Val Ser Glu Met Ala Ser Asn Lys Phe Lys Arg Met Leu
165 170 175

Asn Arg Glu Leu Thr His Leu Ser Glu Met Ser Arg Ser Gly Asn Gln

180 185 190

Val Ser Glu Phe Ile Ser Asn Thr Phe Leu Asp Lys Gln His Glu Val

195 200 205

Glu Ile Pro Ser Pro Thr Gln Lys Glu Lys Glu Lys Lys Arg Pro

210 215 220

Met Ser Gln Ile Ser Gly Val Lys Lys Leu Met His Ser Ser Ser Leu

225 230 235 240

Thr Asn Ser Ser Ile Pro Arg Phe Gly Val Lys Thr Glu Gln Glu Asp

245 250 255

Val Leu Ala Lys Glu Leu Glu Asp Val Asn Lys Trp Gly Leu His Val

260 265 270

Phe Arg Ile Ala Glu Leu Ser Gly Asn Arg Pro Leu Thr Val Ile Met

275 280 285

His Thr Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Lys Ile Pro

290 295 300

Val Asp Thr Leu Ile Thr Tyr Leu Met Thr Leu Glu Asp His Tyr His
305 310 315 320

Ala Asp Val Ala Tyr His Asn Asn Ile His Ala Ala Asp Val Val Gln
 325 330 335

Ser Thr His Val Leu Leu Ser Thr Pro Ala Leu Glu Ala Val Phe Thr
 340 345 350

Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ser Ala Ile His Asp Val
 355 360 365

Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser Glu
 370 375 380

Leu Ala Leu Met Tyr Asn Asp Ser Ser Val Leu Glu Asn His His Leu
385 390 395 400

Ala Val Gly Phe Lys Leu Leu Gln Glu Glu Asn Cys Asp Ile Phe Gln
 405 410 415

Asn Leu Thr Lys Lys Gln Arg Gln Ser Leu Arg Lys Met Val Ile Asp

420

425

430

Ile Val Leu Ala Thr Asp Met Ser Lys His Met Asn Leu Leu Ala Asp

435

440

445

Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val Leu

450

455

460

Leu Leu Asp Asn Tyr Ser Asp Arg Ile Gln Val Leu Gln Asn Met Val

465

470

475

480

His Cys Ala Asp Leu Ser Asn Pro Thr Lys Pro Leu Gln Leu Tyr Arg

485

490

495

Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Arg Gln Gly Asp Arg

500

505

510

Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His Asn

515

520

525

Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val His

530

535

540

Pro Leu Trp Glu Thr Trp Ala Asp Leu Val His Pro Asp Ala Gln Asp
545 550 555 560

Ile Leu Asp Thr Leu Glu Asp Asn Arg Glu Trp Tyr Gln Ser Thr Ile
 565 570 575

Pro Gln Ser Pro Ser Pro Ala Pro Asp Asp Pro Glu Glu Gly Arg Gln
 580 585 590

Gly Gln Thr Glu Lys Phe Gln Phe Glu Leu Thr Leu Glu Glu Asp Gly
 595 600 605

Glu Ser Asp Thr Glu Lys Asp Ser Gly Ser Gln Val Glu Glu Asp Thr
 610 615 620

Ser Cys Ser Asp Ser Lys Thr Leu Cys Thr Gln Asp Ser Glu Ser Thr
625 630 635 640

Glu Ile Pro Leu Asp Glu Gln Val Glu Glu Glu Ala Val Gly Glu Glu
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Glu Glu Ser Gln Pro Glu Ala Cys Val Ile Asp Asp Arg Ser Pro Asp
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Pro Met Thr Ser Pro Gly Ser Gly Leu Ile Leu Gln Ala Asn Phe Val

20 25 30

His Ser Gln Arg Arg Glu Ser Phe Leu Tyr Arg Ser Asp Ser Asp Tyr

35 40 45

Asp Leu Ser Pro Lys Ser Met Ser Arg Asn Ser Ser Ile Ala Ser Asp

50 55 60

Ile His Gly Asp Asp Leu Ile Val Thr Pro Phe Ala Gln Val Leu Ala

65 70 75 80

Ser Leu Arg Thr Val Arg Asn Asn Phe Ala Ala Leu Thr Asn Leu Gln

85 90 95

Asp Arg Ala Pro Ser Lys Arg Ser Pro Met Cys Asn Gln Pro Ser Ile

100 105 110

Asn Lys Ala Thr Ile Thr Glu Glu Ala Tyr Gln Lys Leu Ala Ser Glu

115 120 125

Thr Leu Glu Glu Leu Asp Trp Cys Leu Asp Gln Leu Glu Thr Leu Gln

130 135 140

Thr Arg His Ser Val Ser Glu Met Ala Ser Asn Lys Phe Lys Arg Met

145 150 155 160

Leu Asn Arg Glu Leu Thr His Leu Ser Glu Met Ser Arg Ser Gly Asn

165 170 175

Gln Val Ser Glu Phe Ile Ser Asn Thr Phe Leu Asp Lys Gln His Glu

180 185 190

Val Glu Ile Pro Ser Pro Thr Gln Lys Glu Lys Glu Lys Lys Arg

195 200 205

Pro Met Ser Gln Ile Ser Gly Val Lys Lys Leu Met His Ser Ser Ser

210 215 220

Leu Thr Asn Ser Ser Ile Pro Arg Phe Gly Val Lys Thr Glu Gln Glu
225 230 235 240

Asp Val Leu Ala Lys Glu Leu Glu Asp Val Asn Lys Trp Gly Leu His
 245 250 255

Val Phe Arg Ile Ala Glu Leu Ser Gly Asn Arg Pro Leu Thr Val Ile
 260 265 270

Met His Thr Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Lys Ile
 275 280 285

Pro Val Asp Thr Leu Ile Thr Tyr Leu Met Thr Leu Glu Asp His Tyr
 290 295 300

His Ala Asp Val Ala Tyr His Asn Asn Ile His Ala Ala Asp Val Val
305 310 315 320

Gln Ser Thr His Val Leu Leu Ser Thr Pro Ala Leu Glu Ala Val Phe
 325 330 335

Thr Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ser Ala Ile His Asp
 340 345 350

Val Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser
355 360 365

Glu Leu Ala Leu Met Tyr Asn Asp Ser Ser Val Leu Glu Asn His His
370 375 380

Leu Ala Val Gly Phe Lys Leu Leu Gln Glu Glu Asn Cys Asp Ile Phe
385 390 395 400

Gln Asn Leu Thr Lys Lys Gln Arg Gln Ser Leu Arg Lys Met Val Ile
405 410 415

Asp Ile Val Leu Ala Thr Asp Met Ser Lys His Met Asn Leu Leu Ala
420 425 430

Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val
435 440 445

Leu Leu Leu Asp Asn Tyr Ser Asp Arg Ile Gln Val Leu Gln Asn Met
450 455 460

Val His Cys Ala Asp Leu Ser Asn Pro Thr Lys Pro Leu Gln Leu Tyr
465 470 475 480

Arg Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Arg Gln Gly Asp
 485 490 495

Arg Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His
 500 505 510

Asn Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val
 515 520 525

His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val His Pro Asp Ala Gln
 530 535 540

Asp Ile Leu Asp Thr Leu Glu Asp Asn Arg Glu Trp Tyr Gln Ser Thr
545 550 555 560

Ile Pro Gln Ser Pro Ser Pro Ala Pro Asp Asp Pro Glu Glu Gly Arg
 565 570 575

Gln Gly Gln Thr Glu Lys Phe Gln Phe Glu Leu Thr Leu Glu Glu Asp
 580 585 590

Gly Glu Ser Asp Thr Glu Lys Asp Ser Gly Ser Gln Val Glu Glu Asp
595 600 605

Thr Ser Cys Ser Asp Ser Lys Thr Leu Cys Thr Gln Asp Ser Glu Ser
610 615 620

Thr Glu Ile Pro Leu Asp Glu Gln Val Glu Glu Glu Ala Val Gly Glu
625 630 635 640

Glu Glu Glu Ser Gln Pro Glu Ala Cys Val Ile Asp Asp Arg Ser Pro
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Asp Thr His His His His His His
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10

15

Asn Pro His Cys Pro Asn Pro Trp Leu Asn Glu Asp Leu Val Lys Ser

20 25 30

Leu Arg Glu Asn Leu Leu Gln His Glu Lys Ser Lys Thr Ala Arg Lys

35 40 45

Ser Val Ser Pro Lys Leu Ser Pro Val Ile Ser Pro Arg Asn Ser Pro

50 55 60

Arg Leu Leu Arg Arg Met Leu Leu Ser Ser Asn Ile Pro Lys Gln Arg

65 70 75 80

Arg Phe Thr Val Ala His Thr Cys Lys Leu Phe Asp Val Asp Asn Gly

85 90 95

Thr Ser Ala Gly Arg Ser Pro Leu Asp Pro Met Thr Ser Pro Gly Ser

100 105 110

Gly Leu Ile Leu Gln Ala Asn Phe Val His Ser Gln Arg Arg Glu Ser

115 120 125

Phe Leu Tyr Arg Ser Asp Ser Asp Tyr Asp Leu Ser Pro Lys Ser Met

130 135 140

Ser Arg Asn Ser Ser Ile Ala Ser Asp Ile His Gly Asp Asp Leu Ile
145 150 155 160

Val Thr Pro Phe Ala Gln Val Leu Ala Ser Leu Arg Thr Val Arg Asn
 165 170 175

Asn Phe Ala Ala Leu Thr Asn Leu Gln Asp Arg Ala Pro Ser Lys Arg
 180 185 190

Ser Pro Met Cys Asn Gln Pro Ser Ile Asn Lys Ala Thr Ile Thr Glu
 195 200 205

Glu Ala Tyr Gln Lys Leu Ala Ser Glu Thr Leu Glu Glu Leu Asp Trp
 210 215 220

Cys Leu Asp Gln Leu Glu Thr Leu Gln Thr Arg His Ser Val Ser Glu
225 230 235 240

Met Ala Ser Asn Lys Phe Lys Arg Met Leu Asn Arg Glu Leu Thr His
 245 250 255

Leu Ser Glu Met Ser Arg Ser Gly Asn Gln Val Ser Glu Phe Ile Ser
260 265 270

Asn Thr Phe Leu Asp Lys Gln His Glu Val Glu Ile Pro Ser Pro Thr
275 280 285

Gln Lys Glu Lys Glu Lys Lys Lys Arg Pro Met Ser Gln Ile Ser Gly
290 295 300

Val Lys Lys Leu Met His Ser Ser Ser Leu Thr Asn Ser Ser Ile Pro
305 310 315 320

Arg Phe Gly Val Lys Thr Glu Gln Glu Asp Val Leu Ala Lys Glu Leu
325 330 335

Glu Asp Val Asn Lys Trp Gly Leu His Val Phe Arg Ile Ala Glu Leu
340 345 350

Ser Gly Asn Arg Pro Leu Thr Val Ile Met His Thr Ile Phe Gln Glu
355 360 365

Arg Asp Leu Leu Lys Thr Phe Lys Ile Pro Val Asp Thr Leu Ile Thr
370 375 380

Tyr Leu Met Thr Leu Glu Asp His Tyr His Ala Asp Val Ala Tyr His
385 390 395 400

Asn Asn Ile His Ala Ala Asp Val Val Gln Ser Thr His Val Leu Leu
 405 410 415

Ser Thr Pro Ala Leu Glu Ala Val Phe Thr Asp Leu Glu Ile Leu Ala
 420 425 430

Ala Ile Phe Ala Ser Ala Ile His Asp Val Asp His Pro Gly Val Ser
 435 440 445

Asn Gln Phe Leu Ile Asn Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn
 450 455 460

Asp Ser Ser Val Leu Glu Asn His His Leu Ala Val Gly Phe Lys Leu
465 470 475 480

Leu Gln Glu Glu Asn Cys Asp Ile Phe Gln Asn Leu Thr Lys Lys Gln
 485 490 495

Arg Gln Ser Leu Arg Lys Met Val Ile Asp Ile Val Leu Ala Thr Asp
500 505 510

Met Ser Lys His Met Asn Leu Leu Ala Asp Leu Lys Thr Met Val Glu
515 520 525

Thr Lys Lys Val Thr Ser Ser Gly Val Leu Leu Leu Asp Asn Tyr Ser
530 535 540

Asp Arg Ile Gln Val Leu Gln Asn Met Val His Cys Ala Asp Leu Ser
545 550 555 560

Asn Pro Thr Lys Pro Leu Gln Leu Tyr Arg Gln Trp Thr Asp Arg Ile
565 570 575

Met Glu Glu Phe Phe Arg Gln Gly Asp Arg Glu Arg Glu Arg Gly Met
580 585 590

Glu Ile Ser Pro Met Cys Asp Lys His Asn Ala Ser Val Glu Lys Ser
595 600 605

Gln Val Gly Phe Ile Asp Tyr Ile Val His Pro Leu Trp Glu Thr Trp
610 615 620

Ala Asp Leu Val His Pro Asp Ala Gln Asp Ile Leu Asp Thr Leu Glu
625 630 635 640

Asp Asn Arg Glu Trp Tyr Gln Ser Thr Ile Pro Gln Ser Pro Ser Pro
645 650 655

Ala Pro Asp Asp Pro Glu Glu Gly Arg Gln Gly Gln Thr Glu Lys Phe
660 665 670

Gln Phe Glu Leu Thr Leu Glu Glu Asp Gly Glu Ser Asp Thr Glu Lys
675 680 685

Asp Ser Gly Ser Gln Val Glu Glu Asp Thr Ser Cys Ser Asp Ser Lys
690 695 700

Thr Leu Cys Thr Gln Asp Ser Glu Ser Thr Glu Ile Pro Leu Asp Glu
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725 730 735

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Thr Arg Ala Lys Ser Arg Leu Arg Phe Ser Lys Ser Tyr Ser Lys Leu

20 25 30

Phe Asp Val Asp Asn Gly Thr Ser Ala Gly Arg Ser Pro Leu Asp Pro

35 40 45

Met Thr Ser Pro Gly Ser Gly Leu Ile Leu Gln Ala Asn Phe Val His

50 55 60

Ser Gln Arg Arg Glu Ser Phe Leu Tyr Arg Ser Asp Ser Asp Tyr Asp

65 70 75 80

Leu Ser Pro Lys Ser Met Ser Arg Asn Ser Ser Ile Ala Ser Asp Ile

85

90

95

His Gly Asp Asp Leu Ile Val Thr Pro Phe Ala Gln Val Leu Ala Ser

100

105

110

Leu Arg Thr Val Arg Asn Asn Phe Ala Ala Leu Thr Asn Leu Gln Asp

115

120

125

Arg Ala Pro Ser Lys Arg Ser Pro Met Cys Asn Gln Pro Ser Ile Asn

130

135

140

Lys Ala Thr Ile Thr Glu Glu Ala Tyr Gln Lys Leu Ala Ser Glu Thr

145

150

155

160

Leu Glu Glu Leu Asp Trp Cys Leu Asp Gln Leu Glu Thr Leu Gln Thr

165

170

175

Arg His Ser Val Ser Glu Met Ala Ser Asn Lys Phe Lys Arg Met Leu

180

185

190

Asn Arg Glu Leu Thr His Leu Ser Glu Met Ser Arg Ser Gly Asn Gln

195

200

205

Val Ser Glu Phe Ile Ser Asn Thr Phe Leu Asp Lys Gln His Glu Val
210 215 220

Glu Ile Pro Ser Pro Thr Gln Lys Glu Lys Glu Lys Lys Arg Pro
225 230 235 240

Met Ser Gln Ile Ser Gly Val Lys Lys Leu Met His Ser Ser Ser Leu
245 250 255

Thr Asn Ser Ser Ile Pro Arg Phe Gly Val Lys Thr Glu Gln Glu Asp
260 265 270

Val Leu Ala Lys Glu Leu Glu Asp Val Asn Lys Trp Gly Leu His Val
275 280 285

Phe Arg Ile Ala Glu Leu Ser Gly Asn Arg Pro Leu Thr Val Ile Met
290 295 300

His Thr Ile Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Lys Ile Pro
305 310 315 320

Val Asp Thr Leu Ile Thr Tyr Leu Met Thr Leu Glu Asp His Tyr His
325 330 335

Ala Asp Val Ala Tyr His Asn Asn Ile His Ala Ala Asp Val Val Gln
340 345 350

Ser Thr His Val Leu Leu Ser Thr Pro Ala Leu Glu Ala Val Phe Thr
355 360 365

Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala Ser Ala Ile His Asp Val
370 375 380

Asp His Pro Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser Glu
385 390 395 400

Leu Ala Leu Met Tyr Asn Asp Ser Ser Val Leu Glu Asn His His Leu
405 410 415

Ala Val Gly Phe Lys Leu Leu Gln Glu Glu Asn Cys Asp Ile Phe Gln
420 425 430

Asn Leu Thr Lys Lys Gln Arg Gln Ser Leu Arg Lys Met Val Ile Asp
435 440 445

Ile Val Leu Ala Thr Asp Met Ser Lys His Met Asn Leu Leu Ala Asp
450 455 460

Leu Lys Thr Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val Leu
465 470 475 480

Leu Leu Asp Asn Tyr Ser Asp Arg Ile Gln Val Leu Gln Asn Met Val
485 490 495

His Cys Ala Asp Leu Ser Asn Pro Thr Lys Pro Leu Gln Leu Tyr Arg
500 505 510

Gln Trp Thr Asp Arg Ile Met Glu Glu Phe Phe Arg Gln Gly Asp Arg
515 520 525

Glu Arg Glu Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His Asn
530 535 540

Ala Ser Val Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val His
545 550 555 560

Pro Leu Trp Glu Thr Trp Ala Asp Leu Val His Pro Asp Ala Gln Asp
565 570 575

Ile Leu Asp Thr Leu Glu Asp Asn Arg Glu Trp Tyr Gln Ser Thr Ile
580 585 590

Pro Gln Ser Pro Ser Pro Ala Pro Asp Asp Pro Glu Glu Gly Arg Gln
595 600 605

Gly Gln Thr Glu Lys Phe Gln Phe Glu Leu Thr Leu Glu Glu Asp Gly
610 615 620

Glu Ser Asp Thr Glu Lys Asp Ser Gly Ser Gln Val Glu Glu Asp Thr
625 630 635 640

Ser Cys Ser Asp Ser Lys Thr Leu Cys Thr Gln Asp Ser Glu Ser Thr
645 650 655

Glu Ile Pro Leu Asp Glu Gln Val Glu Glu Glu Ala Val Gly Glu Glu
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675 680 685

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Glu Glu Thr Leu His Ser Ser Asn Glu Glu Glu Asp Pro Phe Arg Gly

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Met Glu Pro Tyr Leu Val Arg Arg Leu Ser Cys Arg Asn Ile Gln Leu

35 40 45

Pro Pro Leu Ala Phe Arg Gln Leu Glu Gln Ala Asp Leu Lys Ser Glu

50 55 60

Ser Glu Asn Ile Gln Arg Pro Thr Ser Leu Pro Leu Lys Ile Leu Pro

65 70 75 80

Leu Ile Ala Ile Thr Ser Ala Glu Ser Ser Gly Lys Leu Phe Asp Val

85 90 95

Asp Asn Gly Thr Ser Ala Gly Arg Ser Pro Leu Asp Pro Met Thr Ser
100 105 110

Pro Gly Ser Gly Leu Ile Leu Gln Ala Asn Phe Val His Ser Gln Arg
115 120 125

Arg Glu Ser Phe Leu Tyr Arg Ser Asp Ser Asp Tyr Asp Leu Ser Pro
130 135 140

Lys Ser Met Ser Arg Asn Ser Ser Ile Ala Ser Asp Ile His Gly Asp
145 150 155 160

Asp Leu Ile Val Thr Pro Phe Ala Gln Val Leu Ala Ser Leu Arg Thr
165 170 175

Val Arg Asn Asn Phe Ala Ala Leu Thr Asn Leu Gln Asp Arg Ala Pro
180 185 190

Ser Lys Arg Ser Pro Met Cys Asn Gln Pro Ser Ile Asn Lys Ala Thr
195 200 205

Ile Thr Glu Glu Ala Tyr Gln Lys Leu Ala Ser Glu Thr Leu Glu Glu
210 215 220

Leu Asp Trp Cys Leu Asp Gln Leu Glu Thr Leu Gln Thr Arg His Ser
225 230 235 240

Val Ser Glu Met Ala Ser Asn Lys Phe Lys Arg Met Leu Asn Arg Glu
 245 250 255

Leu Thr His Leu Ser Glu Met Ser Arg Ser Gly Asn Gln Val Ser Glu
 260 265 270

Phe Ile Ser Asn Thr Phe Leu Asp Lys Gln His Glu Val Glu Ile Pro
 275 280 285

Ser Pro Thr Gln Lys Glu Lys Glu Lys Lys Arg Pro Met Ser Gln
 290 295 300

Ile Ser Gly Val Lys Lys Leu Met His Ser Ser Ser Leu Thr Asn Ser
305 310 315 320

Ser Ile Pro Arg Phe Gly Val Lys Thr Glu Gln Glu Asp Val Leu Ala
 325 330 335

Lys Glu Leu Glu Asp Val Asn Lys Trp Gly Leu His Val Phe Arg Ile
 340 345 350

Ala Glu Leu Ser Gly Asn Arg Pro Leu Thr Val Ile Met His Thr Ile
355 360 365

Phe Gln Glu Arg Asp Leu Leu Lys Thr Phe Lys Ile Pro Val Asp Thr
370 375 380

Leu Ile Thr Tyr Leu Met Thr Leu Glu Asp His Tyr His Ala Asp Val
385 390 395 400

Ala Tyr His Asn Asn Ile His Ala Ala Asp Val Val Gln Ser Thr His
405 410 415

Val Leu Leu Ser Thr Pro Ala Leu Glu Ala Val Phe Thr Asp Leu Glu
420 425 430

Ile Leu Ala Ala Ile Phe Ala Ser Ala Ile His Asp Val Asp His Pro
435 440 445

Gly Val Ser Asn Gln Phe Leu Ile Asn Thr Asn Ser Glu Leu Ala Leu
450 455 460

Met Tyr Asn Asp Ser Ser Val Leu Glu Asn His His Leu Ala Val Gly
465 470 475 480

Phe Lys Leu Leu Gln Glu Glu Asn Cys Asp Ile Phe Gln Asn Leu Thr
 485 490 495

Lys Lys Gln Arg Gln Ser Leu Arg Lys Met Val Ile Asp Ile Val Leu
 500 505 510

Ala Thr Asp Met Ser Lys His Met Asn Leu Leu Ala Asp Leu Lys Thr
 515 520 525

Met Val Glu Thr Lys Lys Val Thr Ser Ser Gly Val Leu Leu Leu Asp
 530 535 540

Asn Tyr Ser Asp Arg Ile Gln Val Leu Gln Asn Met Val His Cys Ala
445 550 555 560

Asp Leu Ser Asn Pro Thr Lys Pro Leu Gln Leu Tyr Arg Gln Trp Thr
 565 570 575

Asp Arg Ile Met Glu Glu Phe Phe Arg Gln Gly Asp Arg Glu Arg Glu
 580 585 590

Arg Gly Met Glu Ile Ser Pro Met Cys Asp Lys His Asn Ala Ser Val
595 600 605

Glu Lys Ser Gln Val Gly Phe Ile Asp Tyr Ile Val His Pro Leu Trp
610 615 620

Glu Thr Trp Ala Asp Leu Val His Pro Asp Ala Gln Asp Ile Leu Asp
625 630 635 640

Thr Leu Glu Asp Asn Arg Glu Trp Tyr Gln Ser Thr Ile Pro Gln Ser
645 650 655

Pro Ser Pro Ala Pro Asp Asp Pro Glu Glu Gly Arg Gln Gly Gln Thr
660 665 670

Glu Lys Phe Gln Phe Glu Leu Thr Leu Glu Glu Asp Gly Glu Ser Asp
675 680 685

Thr Glu Lys Asp Ser Gly Ser Gln Val Glu Glu Asp Thr Ser Cys Ser
690 695 700

Asp Ser Lys Thr Leu Cys Thr Gln Asp Ser Glu Ser Thr Glu Ile Pro
705 710 715 720

Leu Asp Glu Gln Val Glu Glu Glu Ala Val Gly Glu Glu Glu Ser
725 730 735

Gln Pro Glu Ala Cys Val Ile Asp Asp Arg Ser Pro Asp Thr
740 745 750

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Met Ser Ile Ile Met Lys Pro Arg Ser Arg Ser Thr Ser Ser Leu Arg

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Thr Ala Glu Ala Lys Leu Phe Asp Val Asp Asn Gly Thr Ser Ala Gly

20 25 30

Arg Ser Pro Leu Asp Pro Met Thr Ser Pro Gly Ser Gly Leu Ile Leu

35 40 45

Gln Ala Asn Phe Val His Ser Gln Arg Arg Glu Ser Phe Leu Tyr Arg

50 55 60

Ser Asp Ser Asp Tyr Asp Leu Ser Pro Lys Ser Met Ser Arg Asn Ser

65 70 75 80

Ser Ile Ala Ser Asp Ile His Gly Asp Asp Leu Ile Val Thr Pro Phe

85 90 95

Ala Gln Val Leu Ala Ser Leu Arg Thr Val Arg Asn Asn Phe Ala Ala

100 105 110

Leu Thr Asn Leu Gln Asp Arg Ala Pro Ser Lys Arg Ser Pro Met Cys

115 120 125

Asn Gln Pro Ser Ile Asn Lys Ala Thr Ile Thr Glu Glu Ala Tyr Gln

130 135 140

Lys Leu Ala Ser Glu Thr Leu Glu Glu Leu Asp Trp Cys Leu Asp Gln

145 150 155 160

Leu Glu Thr Leu Gln Thr Arg His Ser Val Ser Glu Met Ala Ser Asn

165 170 175

Lys Phe Lys Arg Met Leu Asn Arg Glu Leu Thr His Leu Ser Glu Met
180 185 190

Ser Arg Ser Gly Asn Gln Val Ser Glu Phe Ile Ser Asn Thr Phe Leu
195 200 205

Asp Lys Gln His Glu Val Glu Ile Pro Ser Pro Thr Gln Lys Glu Lys
210 215 220

Glu Lys Lys Lys Arg Pro Met Ser Gln Ile Ser Gly Val Lys Lys Leu
225 230 235 240

Met His Ser Ser Ser Leu Thr Asn Ser Ser Ile Pro Arg Phe Gly Val
245 250 255

Lys Thr Glu Gln Glu Asp Val Leu Ala Lys Glu Leu Glu Asp Val Asn
260 265 270

Lys Trp Gly Leu His Val Phe Arg Ile Ala Glu Leu Ser Gly Asn Arg
275 280 285

Pro Leu Thr Val Ile Met His Thr Ile Phe Gln Glu Arg Asp Leu Leu
290 295 300

Lys Thr Phe Lys Ile Pro Val Asp Thr Leu Ile Thr Tyr Leu Met Thr
305 310 315 320

Leu Glu Asp His Tyr His Ala Asp Val Ala Tyr His Asn Asn Ile His
 325 330 335

Ala Ala Asp Val Val Gln Ser Thr His Val Leu Leu Ser Thr Pro Ala
 340 345 350

Leu Glu Ala Val Phe Thr Asp Leu Glu Ile Leu Ala Ala Ile Phe Ala
 355 360 365

Ser Ala Ile His Asp Val Asp His Pro Gly Val Ser Asn Gln Phe Leu
 370 375 380

Ile Asn Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn Asp Ser Ser Val
385 390 395 400

Leu Glu Asn His His Leu Ala Val Gly Phe Lys Leu Leu Gln Glu Glu
 405 410 415

Asn Cys Asp Ile Phe Gln Asn Leu Thr Lys Lys Gln Arg Gln Ser Leu

420

425

430

Arg Lys Met Val Ile Asp Ile Val Leu Ala Thr Asp Met Ser Lys His

435

440

445

Met Asn Leu Leu Ala Asp Leu Lys Thr Met Val Glu Thr Lys Lys Val

450

455

460

Thr Ser Ser Gly Val Leu Leu Leu Asp Asn Tyr Ser Asp Arg Ile Gln

465

470

475

480

Val Leu Gln Asn Met Val His Cys Ala Asp Leu Ser Asn Pro Thr Lys

485

490

495

Pro Leu Gln Leu Tyr Arg Gln Trp Thr Asp Arg Ile Met Glu Glu Phe

500

505

510

Phe Arg Gln Gly Asp Arg Glu Arg Glu Arg Gly Met Glu Ile Ser Pro

515

520

525

Met Cys Asp Lys His Asn Ala Ser Val Glu Lys Ser Gln Val Gly Phe

530

535

540

Ile Asp Tyr Ile Val His Pro Leu Trp Glu Thr Trp Ala Asp Leu Val
545 550 555 560

His Pro Asp Ala Gln Asp Ile Leu Asp Thr Leu Glu Asp Asn Arg Glu
565 570 575

Trp Tyr Gln Ser Thr Ile Pro Gln Ser Pro Ser Pro Ala Pro Asp Asp
580 585 590

Pro Glu Glu Gly Arg Gln Gly Gln Thr Glu Lys Phe Gln Phe Glu Leu
595 600 605

Thr Leu Glu Glu Asp Gly Glu Ser Asp Thr Glu Lys Asp Ser Gly Ser
610 615 620

Gln Val Glu Glu Asp Thr Ser Cys Ser Asp Ser Lys Thr Leu Cys Thr
625 630 635 640

Gln Asp Ser Glu Ser Thr Glu Ile Pro Leu Asp Glu Gln Val Glu Glu
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Glu Ala Val Gly Glu Glu Glu Glu Ser Gln Pro Glu Ala Cys Val Ile
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Asp Asp Arg Ser Pro Asp Thr

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<211> 809

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<213> Homo sapiens

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Trp Arg His Glu Gln His His Gln Tyr Pro Leu Arg Gln Pro Gln Phe

35 40 45

Arg Leu Leu His Pro His His His Leu Pro Pro Pro Pro Pro Pro Ser

50 55 60

Pro Gln Pro Gln Pro Gln Cys Pro Leu Gln Pro Pro Pro Pro Pro Pro

65 70 75 80

Leu Pro Pro Pro Pro Pro Pro Gly Ala Ala Arg Gly Arg Tyr Ala

85 90 95

Ser Ser Gly Ala Thr Gly Arg Val Arg His Arg Gly Tyr Ser Asp Thr

100 105 110

Glu Arg Tyr Leu Tyr Cys Arg Ala Met Asp Arg Thr Ser Tyr Ala Val

115 120 125

Glu Thr Gly His Arg Pro Gly Leu Lys Lys Ser Arg Met Ser Trp Pro

130 135 140

Ser Ser Phe Gln Gly Leu Arg Arg Phe Asp Val Asp Asn Gly Thr Ser

145 150 155 160

Ala Gly Arg Ser Pro Leu Asp Pro Met Thr Ser Pro Gly Ser Gly Leu

165 170 175

Ile Leu Gln Ala Asn Phe Val His Ser Gln Arg Arg Glu Ser Phe Leu

180 185 190

Tyr Arg Ser Asp Ser Asp Tyr Asp Leu Ser Pro Lys Ser Met Ser Arg

195 200 205

Asn Ser Ser Ile Ala Ser Asp Ile His Gly Asp Asp Leu Ile Val Thr

210 215 220

Pro Phe Ala Gln Val Leu Ala Ser Leu Arg Thr Val Arg Asn Asn Phe
225 230 235 240

Ala Ala Leu Thr Asn Leu Gln Asp Arg Ala Pro Ser Lys Arg Ser Pro
 245 250 255

Met Cys Asn Gln Pro Ser Ile Asn Lys Ala Thr Ile Thr Glu Glu Ala
 260 265 270

Tyr Gln Lys Leu Ala Ser Glu Thr Leu Glu Glu Leu Asp Trp Cys Leu
 275 280 285

Asp Gln Leu Glu Thr Leu Gln Thr Arg His Ser Val Ser Glu Met Ala
 290 295 300

Ser Asn Lys Phe Lys Arg Met Leu Asn Arg Glu Leu Thr His Leu Ser
305 310 315 320

Glu Met Ser Arg Ser Gly Asn Gln Val Ser Glu Phe Ile Ser Asn Thr
 325 330 335

Phe Leu Asp Lys Gln His Glu Val Glu Ile Pro Ser Pro Thr Gln Lys
 340 345 350

Glu Lys Glu Lys Lys Lys Arg Pro Met Ser Gln Ile Ser Gly Val Lys
355 360 365

Lys Leu Met His Ser Ser Ser Leu Thr Asn Ser Ser Ile Pro Arg Phe
370 375 380

Gly Val Lys Thr Glu Gln Glu Asp Val Leu Ala Lys Glu Leu Glu Asp
385 390 395 400

Val Asn Lys Trp Gly Leu His Val Phe Arg Ile Ala Glu Leu Ser Gly
405 410 415

Asn Arg Pro Leu Thr Val Ile Met His Thr Ile Phe Gln Glu Arg Asp
420 425 430

Leu Leu Lys Thr Phe Lys Ile Pro Val Asp Thr Leu Ile Thr Tyr Leu
435 440 445

Met Thr Leu Glu Asp His Tyr His Ala Asp Val Ala Tyr His Asn Asn
450 455 460

Ile His Ala Ala Asp Val Val Gln Ser Thr His Val Leu Leu Ser Thr
465 470 475 480

Pro Ala Leu Glu Ala Val Phe Thr Asp Leu Glu Ile Leu Ala Ala Ile
 485 490 495

Phe Ala Ser Ala Ile His Asp Val Asp His Pro Gly Val Ser Asn Gln
 500 505 510

Phe Leu Ile Asn Thr Asn Ser Glu Leu Ala Leu Met Tyr Asn Asp Ser
 515 520 525

Ser Val Leu Glu Asn His His Leu Ala Val Gly Phe Lys Leu Leu Gln
 530 535 540

Glu Glu Asn Cys Asp Ile Phe Gln Asn Leu Thr Lys Lys Gln Arg Gln
545 550 555 560

Ser Leu Arg Lys Met Val Ile Asp Ile Val Leu Ala Thr Asp Met Ser
 565 570 575

Lys His Met Asn Leu Leu Ala Asp Leu Lys Thr Met Val Glu Thr Lys
 580 585 590

Lys Val Thr Ser Ser Gly Val Leu Leu Leu Asp Asn Tyr Ser Asp Arg
595 600 605

Ile Gln Val Leu Gln Asn Met Val His Cys Ala Asp Leu Ser Asn Pro
610 615 620

Thr Lys Pro Leu Gln Leu Tyr Arg Gln Trp Thr Asp Arg Ile Met Glu
625 630 635 640

Glu Phe Phe Arg Gln Gly Asp Arg Glu Arg Glu Arg Gly Met Glu Ile
645 650 655

Ser Pro Met Cys Asp Lys His Asn Ala Ser Val Glu Lys Ser Gln Val
660 665 670

Gly Phe Ile Asp Tyr Ile Val His Pro Leu Trp Glu Thr Trp Ala Asp
675 680 685

Leu Val His Pro Asp Ala Gln Asp Ile Leu Asp Thr Leu Glu Asp Asn
690 695 700

Arg Glu Trp Tyr Gln Ser Thr Ile Pro Gln Ser Pro Ser Pro Ala Pro
705 710 715 720

Asp Asp Pro Glu Glu Gly Arg Gln Gly Gln Thr Glu Lys Phe Gln Phe
725 730 735

Glu Leu Thr Leu Glu Glu Asp Gly Glu Ser Asp Thr Glu Lys Asp Ser
740 745 750

Gly Ser Gln Val Glu Glu Asp Thr Ser Cys Ser Asp Ser Lys Thr Leu
755 760 765

Cys Thr Gln Asp Ser Glu Ser Thr Glu Ile Pro Leu Asp Glu Gln Val
770 775 780

Glu Glu Glu Ala Val Gly Glu Glu Glu Glu Ser Gln Pro Glu Ala Cys
785 790 795 800

Val Ile Asp Asp Arg Ser Pro Asp Thr
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<211> 1974

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<213> Homo sapiens

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ggcagtcaag tggaagaaga cactagctgc agtgactcca agactctttg tactcaagac 1860

tcagagtcta ctgaaattcc cttgatgaa caggttgaag aggaggcagt aggggaagaa 1920

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36

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<213> Artificial

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<221> 3' primer

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<211> 61

<212> DNA

<213> Artificial

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<221> 6His

<222> (1)..(61)

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61